



## otulipenia

Otulipenia is characterized by abnormal inflammation throughout the body. Inflammation is a normal immune system response to injury and foreign invaders (such as bacteria). However, the uncontrolled inflammation that occurs in otulipenia can damage many of the body's tissues and organs, including the gastrointestinal system, joints, and skin. Disorders such as otulipenia that result from abnormally increased inflammation are known as autoinflammatory diseases.

Signs and symptoms of otulipenia usually begin within the first few weeks of life, with recurring episodes of fever; diarrhea; painful, swollen joints; and skin rashes. The skin rashes are due to inflammation of the layer of fatty tissue under the skin (panniculitis), which causes painful red bumps. Some people with otulipenia have an abnormal distribution of fatty tissue in their bodies (lipodystrophy). Affected infants have difficulty growing and gaining weight at the expected rate (failure to thrive). Damage to the body's tissues and organs caused by inflammation is life-threatening if the condition is not treated.

### Frequency

The prevalence of otulipenia is not known. At least four cases have been reported in the medical literature.

### Genetic Changes

Otulipenia is caused by mutations in the *OTULIN* gene. The protein produced from this gene helps control inflammation. Inflammation can be turned on by a cellular process called ubiquitination, in which molecules called ubiquitin are attached to certain proteins. In particular, signaling pathways that lead to inflammation are stimulated by the attachment of chains of ubiquitin molecules linked end-to-end (linear ubiquitin chains). The OTULIN protein helps control inflammation by removing these linear ubiquitin chains.

*OTULIN* gene mutations that cause otulipenia lead to production of an OTULIN protein with reduced function. As a result, removal of linear ubiquitin chains is impaired, and signaling pathways that cause inflammation are abnormally active. The excessive inflammation that results causes fever, diarrhea, panniculitis, and the other signs and symptoms of otulipenia.

### Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal

recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

### **Other Names for This Condition**

- AIPDS
- autoinflammation, panniculitis, and dermatosis syndrome
- ORAS
- OTULIN-related autoinflammatory syndrome

### **Diagnosis & Management**

#### Genetic Testing

- Genetic Testing Registry: AUTOINFLAMMATION, PANNICULITIS, AND DERMATOSIS SYNDROME  
<https://www.ncbi.nlm.nih.gov/gtr/conditions/CN238359/>

#### General Information from MedlinePlus

- Diagnostic Tests  
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy  
<https://medlineplus.gov/drugtherapy.html>
- Genetic Counseling  
<https://medlineplus.gov/geneticcounseling.html>
- Palliative Care  
<https://medlineplus.gov/palliativecare.html>
- Surgery and Rehabilitation  
<https://medlineplus.gov/surgeryandrehabilitation.html>

### **Additional Information & Resources**

#### MedlinePlus

- Encyclopedia: Immune Response  
<https://medlineplus.gov/ency/article/000821.htm>
- Health Topic: Autoimmune Diseases  
<https://medlineplus.gov/autoimmunediseases.html>

### Additional NIH Resources

- National Institute of Arthritis and Musculoskeletal and Skin Diseases: Autoinflammatory Diseases  
[https://www.niams.nih.gov/Health\\_Info/Autoinflammatory/](https://www.niams.nih.gov/Health_Info/Autoinflammatory/)
- National Institutes of Health News Releases: NIH Researchers Discover Otulipenia, a New Inflammatory Disease  
<https://www.nih.gov/news-events/news-releases/nih-researchers-discover-otulipenia-new-inflammatory-disease>

### Educational Resources

- Cambridge University Hospitals (UK): Lipodystrophy  
[http://www.cuh.org.uk/sites/default/files/publications/PIN3418\\_lipodystrophy\\_v1.pdf](http://www.cuh.org.uk/sites/default/files/publications/PIN3418_lipodystrophy_v1.pdf)
- Merck Manual Consumer Version: Panniculitis  
<https://www.merckmanuals.com/home/skin-disorders/hypersensitivity-and-inflammatory-skin-disorders/panniculitis>
- NHS Choices (UK): Panniculitis  
<http://www.nhs.uk/Conditions/panniculitis/Pages/Panniculitis.aspx>

### Patient Support and Advocacy Resources

- Autoinflammatory Alliance  
<http://www.autoinflammatory-search.org/>
- Stop Childhood Autoinflammatory Diseases Now  
<http://www.stopcaidnow.org/>

### Scientific Articles on PubMed

- PubMed  
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28otulin+deficiency%29+OR+%28otulipenia%29%29+AND+english%5Bla%5D+AND+%22last+3600+days%22%5Bdp%5D>

### OMIM

- AUTOINFLAMMATION, PANNICULITIS, AND DERMATOSIS SYNDROME  
<http://omim.org/entry/617099>

## Sources for This Summary

- Damgaard RB, Walker JA, Marco-Casanova P, Morgan NV, Titheradge HL, Elliott PR, McHale D, Maher ER, McKenzie AN, Komander D. The Deubiquitinase OTULIN Is an Essential Negative Regulator of Inflammation and Autoimmunity. *Cell*. 2016 Aug 25;166(5):1215-1230.e20. doi: 10.1016/j.cell.2016.07.019.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/27523608>  
*Free article on PubMed Central:* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5002269/>
- Elliott PR, Komander D. Regulation of Met1-linked polyubiquitin signalling by the deubiquitinase OTULIN. *FEBS J*. 2016 Jan;283(1):39-53. doi: 10.1111/febs.13547. Review.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/26503766>  
*Free article on PubMed Central:* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4765238/>
- Keusekotten K, Elliott PR, Glockner L, Fiil BK, Damgaard RB, Kulathu Y, Wauer T, Hospenthal MK, Gyrd-Hansen M, Krappmann D, Hofmann K, Komander D. OTULIN antagonizes LUBAC signaling by specifically hydrolyzing Met1-linked polyubiquitin. *Cell*. 2013 Jun 6;153(6):1312-26. doi: 10.1016/j.cell.2013.05.014.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/23746843>  
*Free article on PubMed Central:* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3690481/>
- Zhou Q, Yu X, Demirkaya E, Deutch N, Stone D, Tsai WL, Kuehn HS, Wang H, Yang D, Park YH, Ombrello AK, Blake M, Romeo T, Remmers EF, Chae JJ, Mullikin JC, Güzel F, Milner JD, Boehm M, Rosenzweig SD, Gadina M, Welch SB, Özen S, Topaloglu R, Abinun M, Kastner DL, Aksentijevich I. Biallelic hypomorphic mutations in a linear deubiquitinase define otulipenia, an early-onset autoinflammatory disease. *Proc Natl Acad Sci U S A*. 2016 Sep 6;113(36):10127-32. doi: 10.1073/pnas.1612594113.  
*Citation on PubMed:* <https://www.ncbi.nlm.nih.gov/pubmed/27559085>  
*Free article on PubMed Central:* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5018768/>

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